

The Anthrax Vaccine and the United States Military: The Ethics of Anthrax Vaccine
Administration and Informed Consent

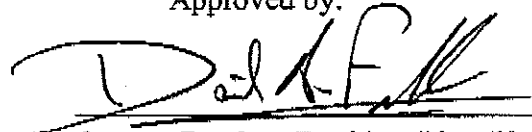
by

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Abstract

The anthrax bacterium, when converted into a biological weapon, poses a serious threat to the United States military forces in battle. In order to counteract this threat, the Department of Defense (DoD) instituted the Anthrax Vaccine Immunization Program (AVIP), which mandates that all military forces take the anthrax vaccine shot series. There has been a wave of controversy over this program, because the vaccine has not been proven as safe and effective against the strains of anthrax that would potentially be encountered in warfare.

The controversy over the program has been surrounded by discussions of whether or not the military should be required to sign an informed consent form when given the vaccine, in order to ensure that they fully understand the potential benefits and risks associated with the vaccine and still choose to take the shot. The DoD maintains that the vaccine is completely safe and efficacious, and that because the vaccine is licensed, no informed consent is required. The military and civilians counter this argument by stating that the vaccine is not being used for the condition that it was tested for, and is therefore still considered to be an investigational drug. In order to administer an investigational drug, and informed consent must be obtained.

Many legal battles are being fought, both by military men and women wishing to reverse their discharges because of refusing the vaccine, and by military men and women who have experienced serious side effects as a result of the vaccine. There are also legislative actions being proposed, but nothing thus far has been approved. A reasonable solution would be to make the AVIP program voluntary until a better vaccine is developed and the long-term effects are more fully understood. This would allow the military personnel to make the personal decision of what medication they want to put into their bodies, and to be fully informed of the benefits and risks associated with that medication before the vaccine is administered.

Though countries have been studying and developing biological weapons for years, the events of September 11, 2001 introduced the threat to the entire world. Letters infested with the anthrax bacterium began to surface around the United States, causing a newfound fear in American citizens regarding biological and chemical warfare. By this time, however, the military had already put an anthrax vaccine program into place and was in the process of trying to vaccinate all of the troops against this bioweapon. A controversy and outcry from the military personnel ensued, due to the fact that many troops that took the anthrax vaccine experienced adverse health effects, varying in severity. Troops continue to refuse the vaccine and suffer the consequences, and so the debate continues on whether it is ethical to have a mandatory anthrax vaccination program for the United States military forces, especially when the long-term effects of the vaccine are unknown and have not been conclusively studied. In addition, the vaccine is currently only tested and approved for cutaneous anthrax, not the inhalation form that would be experienced in combat (Nicolson, Nass, and Nicolson, 2000)

The issues surrounding this controversy will be discussed, including an overview of the anthrax bacterium, the history of the vaccine's development, safety and efficacy, the history of the military's adoption of the vaccine, and current issues involving the military officials, troops, scientists, and pending legislation. The existing problem is that there is not enough hard evidence to support giving this vaccine to our troops without knowing all of the potential consequences. Because the administration of the vaccine for inhalation anthrax is still investigational, it should be treated as such by the Food and Drug Administration (FDA) and the military and informed consent should be obtained from the recipients of the vaccine. If the vaccine is continually administered as is, the military risks losing more soldiers to side effects of the vaccine and also to the fear of taking the vaccine in the first place. In a time as crucial as

this, we cannot afford to lose troops, but should provide them with the latest information on the vaccine and its known side effects, then let them make their own decision on whether or not they will take the vaccine.

The Anthrax Bacterium

The biological weapon (BW) commonly known to scientists as *Bacillus anthracis* is a spore-forming soil bacterium that is endogenous in some parts of the world, but rarely found in the United States. The scientific name for the bacterium is derived from the Greek word *anthrakis*, which means coal, because the disease causes black, coal-like lesions to erupt on the body (Inglesby et al., 1999). Naturally occurring anthrax is a disease that is acquired through contact with animals that have anthrax or with any contaminated animal products that are anthrax infested. The disease is primarily found in herbivores, which ingest the spores from the soil when eating plant life. Infection with this bacterium can induce death within one to six days of exposure to a lethal dose (Nicolson, n.d.).

Forms of Anthrax

The serious forms of anthrax that can be transmitted to humans are inhalation, cutaneous, and intestinal anthrax. Inhalation anthrax symptoms usually resemble a common cold in the early stages of infection, and then progress to severe respiratory problems and shock. Once the bacteria are in the body and begin replicating and releasing toxins, the body responds with hemorrhaging, edema, and necrosis. Even if antibiotics are administered and they neutralize the bacteria in the bloodstream, there is a point where the toxins become so powerful that death cannot be avoided by any means. Early diagnosis of inhalation anthrax is difficult, and can only

be caught with a high level of suspicion on the part of the practitioner. Cutaneous anthrax is a result of the introduction of the anthrax spore through the skin; people with previous cuts and abrasions are the most susceptible to infection. Areas of exposed skin, such as the arms, face, hands, and neck, are the most commonly affected. It is the most common naturally occurring form of anthrax, with over 2000 cases reported annually (Inglesby et al., 1999). This form of the disease usually follows exposure to anthrax-infested animals. The mortality rate has been reported as up to 20% for cases without antibiotic treatment, however with antibiotics, death from cutaneous anthrax is rare. The intestinal form may be contracted from contaminated food consumption, and is evident by an inflammation of the intestinal tract. The treatment is similar to that of the aggressive regimen seen in inhalation anthrax, and the mortality rate is reported to be high because of difficulty in early diagnosis. If untreated, all forms of anthrax infection can lead to septicemia and death (Inglesby et al., 1999).

Anthrax as a Biological Weapon

In its spore form, the anthrax bacterium exhibits all of the qualities of an effective biological weapon. It is highly infectious, very pathogenic, and stable in the air and environment for the period of time needed to disseminate and infect large numbers of people. Anthrax is considered very threatening as a lethal biological weapon because it is easily produced, stored and disseminated in its spore form (Nicolson et al., 2000). The most recent incident that has raised the awareness of the American public was the anthrax-infested letters being sent through the US Postal Service shortly after the attack on the World Trade Center in 2001. The anthrax was sent in at least five letters to Florida, New York City, and Washington DC. These letters were sent from an unknown source to prominent people such as news anchormen, politicians, and other

public officials. In all, there were twenty-two confirmed or suspected cases of anthrax in the aftermath of 9/11, as a result of direct or indirect contact with the infected letters. Eleven of the cases were inhalation anthrax, 5 of which subsequently died, and eleven of the cases were cutaneous anthrax (7 confirmed, 4 suspected) (Inglesby et al., 2002). It is important to note that the person(s) responsible for the anthrax mailings utilized only one of the many possible avenues to distribute anthrax.

Both the World Health Organization and the Office of Technology Assessment have studied the technology that might facilitate a large aerosol release of anthrax. Prior to the anthrax attacks in 2001, the only sources of information on inhalation anthrax were an epidemic in Sverdlovsk, Russia due to an unintended release of anthrax spores from a Soviet bioweapons facility in 1979, and 18 occupational exposure cases in the US during the 20th century. An aerosol attack using anthrax would be odorless and invisible, and would be able to travel many miles before dissipating. The technology necessary to facilitate such an aerial release has been developed and tested by both Iraq and the former Soviet Union. Both the World Health Organization (WHO) and the Office of Technology Assessment have conducted studies regarding the spread of anthrax when distributed in this manner, and the results are staggering. One estimate said that if 50kg of anthrax were released over an urban population of around five million people, it would result in 250,000 sick people and 100,000 deaths. Another study resulted in a 32-mile long line of anthrax being sprayed, which subsequently traveled more than 60 miles before it became non-infectious (Inglesby, et al., 2002). The 2001 anthrax attacks have served to raise awareness as well as paranoia that a terrorist group could potentially mount a large-scale aerosol bioweapons attack against the United States.

Research on anthrax as a bioweapon began over 80 years ago, but most national offensive bioweapons programs were terminated following the ratification of the Biological Weapons Convention (BWC) in the 1970's. However, some countries continued their development of these weapons in spite of their ratification of the BWC. Iraq acknowledged that they maintained an anthrax production and weaponizing program to the United Nations Special Commission in 1995. Another country that is known to have maintained production of anthrax is the former Soviet Union (Inglesby, et al., 2002). According to a recent analysis, there is still a high potential that at least 13 countries have continued to house offensive biological weapons (Center for Nonproliferation Studies, 2002).

Methods to Counter Anthrax

There are currently several methods to counter anthrax when used as a biological weapon. First of all, there are prophylactic antibiotics. In order to be effective, these antibiotics must be administered within a short period of time before or after anthrax exposure. However, once a person infected with the anthrax bacteria has begun to show signs of illness, the antibiotics can no longer prevent a lethal infection. The second option is passive immunization, which entails the administration of immune sera or monoclonal antibodies, which are not currently available. This administration must be done in a hospital or other monitored environment, as the mode of entry is typically intravenous. Active vaccination is the third option, which is appealing because as long as immunity is maintained, the vaccine can be given years before exposure and still be considered effective. Its effectiveness is maintained as long as enough immunity is built up to neutralize the anthrax bacteria before the pattern of mass replication from its inactive spore form initiates and lethal toxins are deposited into the body (Nicolson et al., 2000).

History of Anthrax Vaccine Development and Efficacy

Though the active vaccination method may sound like the most promising method of protection against the anthrax bacteria, the vaccine as it currently exists may not be up to the task. Although the vaccine can protect against small doses of the anthrax bacteria that can infect surface skin wounds, there is no scientific evidence that the current anthrax vaccine, which is the topic of so much controversy, will actually immunize humans against a lethal aerosol dose of inhalation anthrax spores. Animal studies have been performed, however there are no human studies that can estimate the long-term effects of this vaccine on human beings. The Department of Defense has repeatedly stated that this vaccine is safe and effective, however they insist on using it off-label by indicating that it is effective against inhalation anthrax, when the vaccine is only approved for use against cutaneous anthrax. The vaccine has a history that began with wool workers that were exposed to anthrax (Sidel, Cohen & Gould, 2002).

The Anthrax Vaccine History

A man named George Wright developed the original anthrax vaccine in the 1950's, and this vaccine was mass-produced by Merck (*Medical Readiness, 1999*). In 1962, Brachman and his colleagues working at what was then known as the Communicable Disease Center were able to perform a controlled trial of a version of the anthrax vaccine. The results of this trial showed that the vaccine as it existed was effective in preventing cutaneous anthrax in woolen mill workers (Sidel et al., 2002). After this study, the manufacturing process on the original vaccine was changed, and the Michigan Department of Public Health (MDPH) began producing the vaccine (*Medical Readiness, 1999*). In the original trial performed by Brachman, there were not

enough cases of inhalation anthrax to satisfactorily deduce that the vaccine would prove effective in preventing this type of anthrax infection. To infect humans with inhalation anthrax on purpose would obviously be unethical, however several animal studies have suggested that there is a chance the vaccine may be able to prevent inhalation anthrax. Based on these inconclusive studies alone, the Department of Defense began using the vaccine for that “off-label” purpose (Sidel et al., 2002).

A major concern related to the anthrax vaccine is the source. Many of the military vaccines administered to our service people are from ‘sole-source’ manufacturers, thus making it difficult to obtain specific information on the anthrax vaccine and how it was determined to be safe. The FDA mandates that many strict production and safety requirements must be met, and evidence for effectiveness in humans should be documented prior to the FDA releasing approval for production and sale of the vaccine. In the case of the current anthrax vaccine, however, there seems to be several faults with this system (Nicolson et al., 2000).

The original producer of this vaccine was Michigan Biologic Products, Inc. of the Michigan State Department of Health, which is a state-owned corporation that obtained U. S. Government approval for the anthrax vaccine before FDA approval was required. The Bureau of Biologics at NIH approved the anthrax vaccine developed by Michigan Biologic Products, Inc. in 1970, two years before efficacy data were reviewed and approval required by the FDA. At the time of submission, no long-term safety data were supplied with the license application, and none have been submitted to this day (Nicolson et al., 2000).

Michigan Biologic Products Inc. (MBPI) had been warned by the FDA of their intent to revoke their license to produce vaccines because of violations regarding their production and testing methods. On March 11, 1997, the FDA issued a warning letter to MBPI, stating that their

license would be revoked unless immediate action was taken to resolve deficiencies. The FDA cited numerous problems with equipment, control of components, drug product containers and closures, production and process controls, and laboratory controls (*FDA Warns, 1997*). Though MBPI received a written notification from the FDA that they had not complied with the requirements to address the violations as issued in their report, they were allowed to remain open for business with a waiver, pending FDA compliance. This waiver was granted with the rationale that they were the sole manufacturer of the anthrax vaccine. During this time, anthrax vaccine lots were distributed to the military. These lots were later re-tested and only 6 of the 31 lots passed initial supplemental inspection. Many of the lots had either expired or had been re-dated for an additional 3 years once or even twice in some cases. The British Gulf War veterans, after having the vaccine lots independently tested, reported that they appeared to be contaminated with “unknown microorganisms,” thus indicating that some of the health problems associated with this vaccine could have been related to possible vaccine contamination within MBPI (Nicolson et al., 2000).

Bioport, Inc. has since purchased the original license for the anthrax vaccine and the facility of Michigan Biologic Products, Inc. of the Michigan State Department of Health. This new company is owned by a group of investors lead by Admiral William Crowe, Jr., former head of the Joint Chiefs of Staff, DOD, and Faud El-Hibri, a German citizen of Lebanese descent who has since obtained American citizenship. Bioport, Inc. was sold to Admiral Crowe’s investment group after the decision was made by the DOD to utilize the anthrax vaccine on all of the U. S. armed forces. This and other issues that have arisen have motivated a congressional investigation into the financial relationship between the DOD and the new owners of Bioport, Inc., and the possibility of a conflict of interest (Nicolson et al., 2000).

In September of 2000, according to Williams (2000), Bioport Inc. was cited for using an expired lot of the vaccine; they had failed to gain the FDA's approval to produce new lots of the vaccine. Rep. Christopher Shays (R-Conn.) stated that the "Pentagon is locked in a dependent relationship with a new, unproven company. Resting on so weak a foundation, the anthrax vaccine program may not be safe or sustainable" (Daniels, 1999). Shays continued by referring back to the Government Reform Committee Report and its assessment that the anthrax vaccine is still in the investigational stages in relation to the defense against biological warfare. He specifically criticized the Department of Defense for showing favoritism towards the vaccine's manufacturer, Bioport Inc, and warned that they may not survive the FDA's investigations and strict standards outside of this government vaccine contract (Eberhart, 2001a).

Efficacy of the Anthrax Vaccine

The original vaccine, developed by George Wright, was tested on mill workers and found to be efficacious when used for cutaneous anthrax. In contrast, however, the vaccine licensed in 1970 has only been tested for efficacy in animals. These animal studies have focused primarily on determining the levels of protection that the licensed vaccine can offer against inhalation anthrax. Although the animal studies have shown some promising results, it would be erroneous to assume that these results mean that the vaccine would also be effective to protect humans against inhalation anthrax (*Medical Readiness, 1999*).

The study conducted by Brachman is the only one that tests the efficacy of the anthrax vaccine on humans, and uses the original vaccine (developed by Wright). However, because this vaccine is different from the vaccine that was eventually licensed, additional data were required to be submitted to the Division of Biologics, Department of Health, Education, and Welfare

(HEW) in support of the license application for the altered vaccine in 1969. The HEW committee decided that the data were inconclusive and efficacy could not be assumed. The Army also weighed in on the issue in 1991, stating that it cannot be scientifically assumed that the vaccine would be effective if used under different circumstances than those in which the original trial was performed. The only assumption that can logically be made is that the epidemiological evidence from the original vaccine can be applied to the licensed (MDPH) vaccine, and that the licensed vaccine is effective in protecting against cutaneous anthrax. In order to prove protection against inhalation anthrax, however, more testing must be performed specifically on that indication (*Medical Readiness, 1999*).

There are many questions surrounding the anthrax vaccine's efficacy, particularly when different biological weapons are combined to make an overwhelming weapon. This vaccine has been and continues to be administered by the military to over one million men and women, and the military claims that it is highly effective against biological weapons. This claim essentially refers to the vaccine's effectiveness against weaponized anthrax, which consists of strains of the bacteria that have been altered to be more highly pathogenic and evasive than the strains found in the environment. However, there is no published scientific evidence that this claim is true. The existing published data do not cover the effectiveness of different vaccines when a human inhales anthrax spores, and the data do not address highly pathogenic strains of the bacteria that would most likely be in a bioweapon attack (Nicholson, n.d.).

In addition, there are currently no published scientific studies that are meant to test the hypothesis that vaccines are able to protect against simultaneous exposure to multiple aerosolized agents, or that there is even a vaccine that protects an individual against all strains of a given biological agent (Nicholson, n.d.). The trend in biological warfare is the "Russian doll

cocktail,” which combines multiple microorganisms plus macrophages and other inhibitors in order to break down the body’s first line of defense. The Secretary of the Army, Louis Caldera, concluded that there is no way to know for certain that the anthrax being tested in our studies of efficacy will be the same strains that are encountered in warfare (Daniels, 1999).

Military Adoption of the Anthrax Vaccine and Health Consequences

In an effort to respond to the growing threat of bioterrorism and biological weapons being used against the military, in 1998 the Department of Defense launched the Anthrax Vaccine Immunization Program, more commonly known as AVIP. This program mandated a force-wide, mandatory anthrax vaccination and maintenance of the immunization with the required booster shots over a period of 18 months. Numerous sources spoke out against the DOD’s program, citing that the efficacy of the anthrax vaccine has not been proven and the potential for adverse experiences in the vaccine recipients is not fully understood (Sidel et al., 2002). As a result, this program has been heavily criticized, and in response to service members complaining about the insensitivity to adverse health effects, poor medical record keeping and overpowering program operation, the House Government Reform Committee initiated an oversight investigation into the design and implementation of the AVIP (House Committee, 2000). The committee operated under the philosophy that the anthrax vaccine is still being studied as a potential causative or contributing factor in Gulf War veterans’ illnesses, and therefore should be measured against the standard that continued use of the vaccine should be carefully explored and only used as necessary. After the investigation, their conclusion was that the vaccine program did not meet either criterion, and in fact, failed miserably. According to the report, the AVIP does not have a stable standard of care and tries to reach those who are not at risk in addition to those that are at

risk (House Committee, 2000). The report goes on further to state that as a mandatory, force-wide countermeasure to the real threat of weaponized anthrax on the battlefield the vaccine effort is unrealistic. It expands and distorts the use of invasive, dated medical technology to address perceived weaknesses in detection technology and external physical protection against biological attack. The report describes the AVIP as a huge military undertaking that is built on a shaky scientific and medical foundation (House Committee, 2000). The aforementioned Shay's report directly addresses the fact that there is no reliable information regarding how much protection the vaccine offers, who is able to acquire this protection, and how long the protection will last. The amazing amount of faith that the Department of Defense is marketing is being backed up with a miniscule amount of scientific proof. Many of the men and women of the armed forces do not share this faith in the vaccine and the associated program. The House Government Reform Committee Report suggests that the military personnel are not convinced that the small amount of evidence related to vaccine efficacy outweighs the potential for problems in the long term with the safety of the vaccine (House Committee, 2000).

The AVIP program was poorly planned and even more poorly executed, leaving little room for flexibility. In order to achieve military objectives, the AVIP program has been accused of sacrificing the quality of care and the practice of medicine (House Committee, 2000). Instead of pursuing the development of a better vaccine, or at the very least, a shorter inoculation schedule, the AVIP was launched without regard to the repercussions that could affect the men and women of the military. Instead, they went forward with using a 1950's era vaccine, which requires a lengthy inoculation period of six shots over 18 months. This task in and of itself is overwhelming, considering the 2.4 million active duty and reserve members of the armed forces. In short, Shay's report dictates that the military's vaccination program is a logistical nightmare,

and cannot succeed as it is currently organized (House Committee, 2000). Shay himself stated, “In the early 1990s, the Department of Defense faced a fork in the road to effective force protection and picked the wrong path” (Williams, 2000).

APHA Recommendations

In response to the growing controversy regarding the anthrax vaccine and its potential effects on the men and women of the military, the American Public Health Association released the following recommendations:

1. The US Department of Defense should delay any further immunization against anthrax using the current vaccine or at least make immunization voluntary; and
2. A commission of military and non-military public health experts should be formed to review the evidence for effectiveness and safety of the current vaccine and the time at which an improved vaccine may be available, and to make recommendations about the continuation of the current immunization program (*Anthrax Immunization*, 1999).

Anthrax Vaccine Safety

Safety remains at the top of the list of concerns surrounding the anthrax vaccine. The AVIP program is under increasing attack, led by at least 1,500 service people that have complained of side effects with varying severity that they blame on the vaccine (Williams, 2000). Hundreds of the service people have chosen not to be inoculated as a result of these fears, and have been either disciplined or discharged. Rather than take the inoculations, members of the reserve and National Guard simply resigned, followed by at least 250 military pilots. According to Williams (2000), there is no way to know the exact number of soldiers that have suffered from adverse

reactions to the anthrax vaccination, and no way to know how many of those reactions should be considered either severe or long-term. The question remains, why are so many of our armed forces refusing this vaccine, and putting their jobs on the line to take such a stand? The bottom line, according to several sources, is that there is no evidence that the current anthrax vaccine will be effective or safe in stopping a lethal dose of weaponized anthrax spores (Nicholson et al., 2000). The U. S. Army Medical Research Institute for Infectious Disease (USAMRIID) has stated that the anthrax vaccine is safe, citing an adverse reaction rate of one per 50,000 doses (less than 0.002%). However this rate has since been revised to 0.02-0.2% or higher, and these rates are currently being questioned as well. Dover Air Force Base, for example, has a rate of chronic health problems after receiving the anthrax vaccine that may be as high as 7%. The difference is that the official rates are for acute reactions only (Nicolson et al., 2000).

The primary method of assessing a vaccine's safety is for the FDA to carefully review the reported adverse events collected through the Vaccine Adverse Event Reporting System (VAERS). According to standard procedure, a FDA-approved contractor should independently record these adverse events. The contractor sends this data to the FDA, where a committee evaluates the adverse events for the likelihood of their being caused by the vaccination. In the case of the anthrax vaccine, however, the military physicians were told that only certain adverse events could be attributable to the vaccine, including allergic reactions (localized at the injection site), and that other reactions such as joint pain or cognitive disturbances could not be caused by the vaccine. In addition, the attending physicians had no access to published data on the side effects of the anthrax vaccine, and the Physicians Desk Reference contained no entry for this vaccine. Because of this procedure, only reactions that resulted in hospitalization or immediate loss of 24 hours of duty time were reported to a military clearing-house for vaccine reactions.

This procedure has changed recently, and the hope is that other adverse vaccine effects will now be recorded in the patient's medical records. Many sources believe that the anthrax vaccine is no different from any other commercial vaccine, and should be treated as such in the process of safety evaluation (Nicolson et. al., 2000).

Adverse Event Reporting

Adverse event reporting becomes yet another problem when faced with the facts that many of our service people afflicted with adverse anthrax vaccine reactions are reluctant to seek medical care, as they have watched their colleagues' concerns being attributed to depression or stress. Another fear of reporting such adverse events is that they could potentially lose their ability to perform their duties. For example, many of the pilots and airmen at Dover Air Force Base are now on DNIF (duties not including flying) status because of undiagnosed illnesses that began after they received their anthrax vaccinations (Nicolson et al., 2000).

Lt. Colonel Randy Randolph, director of the U. S. Army's vaccination program, describes adverse events beyond those at the injection site as muscle aches, joint aches, headaches, rash, chills, fever, nausea, loss of appetite, malaise, or related symptoms, and that they are experienced by 5% up to 35% of people receiving the vaccine. One study sought to determine the outcome of anthrax administration in a military field hospital. The results showed that the prevalence of adverse reactions to the anthrax vaccine was higher than expected, and the initial affect on the military was the incapacitation of around 18% of the personnel. Because many of the military personnel do not want to comply with further vaccines after the initial reaction, the immunization strategy needs to be revisited in order to encourage better compliance and safety (Hayes, 2000). No completed studies exist that document the long-term effects of this vaccine on humans.

There is a distinct difference between military and civilian physicians in their acceptance of the possibility that a vaccine can potentially cause an adverse event even after the initial vaccine reporting period. Dover AFB personnel exhibited a higher than normal rate of signs and symptoms that can surface well after the vaccine adverse event reporting period, such as vomiting, diarrhea, polyarthralgias, fever, splenic tenderness, cognitive problems, polymyalgias, and weakness and numbness. There are several groups of individuals that are more susceptible to an adverse reaction to the vaccine, including those that have preexisting autoimmune conditions such as rheumatoid arthritis, lupus, multiple sclerosis, or those with neurological disease such as childhood polio (Nicolson et al., 2000).

There have been several reports of very serious, life-threatening reactions in military personnel after anthrax vaccination, such as an allergic reaction that causes the loss of skin and the lining of the GI tract, or even seizures with complete loss of consciousness. Many of these symptoms have not been previously identified as potential side effects of other vaccines, and many of the people reporting such symptoms and side effects have not had a complete physical examination (including immunological testing). Therefore, it is unclear exactly how the anthrax vaccine may be causing such illnesses. Garth Nicolson, the Chief Scientific Officer and Professor at The Institute for Molecular Medicine, holds the belief that the practice of vaccinating military personnel with multiple immunizations at one time could result in immune suppression of the individual's system. This immunosuppression can lead to any number of opportunistic infections that may not have otherwise manifested themselves (Nicolson, n.d.).

Military Personnel Reaction to Anthrax Vaccine

The members of the military have been very vocal regarding the issues surrounding the vaccination program. Though the resistance to the vaccine is still small, the Pentagon is being forced to deal with increasing numbers of soldiers refusing the vaccine. Only a small number of the military personnel that are required to receive the beginning of the anthrax shot regimen and have refused have subsequently been punished. The Pentagon currently dismisses the resistance as insignificant, but the officials have stopped their count of how many military personnel have refused the vaccine (Myers, 1999).

The refusals of the anthrax vaccine began with military personnel in areas such as the Pacific and the Persian Gulf, who were the first in line to receive this vaccination due to their close proximity to North Korea and Iraq. As the vaccination program moves into the United States military bases, the rebellion against the vaccine is believed to be growing. The General Accounting Office (a division of the Congress) reported that around 4,400 pilots and crew in the air force and air national guard have either resigned their position or requested reassignment in order to eliminate the possibility of taking the anthrax vaccine. It is estimated that around 18% of the aircrew left the service even though they did not yet qualify for retirement benefits, due to the fears of side effects from the vaccine (Charatan, 2000). The anthrax vaccination is an order, and to refuse the order is to incur punishment. Because the shots cannot be forced upon the troops, many of the ones who have refused have been discharged under either the general heading or in some cases, bad conduct.

There are many reasons why military men and women are refusing the vaccine, particularly that there is not currently a way to test the anthrax vaccine on the same type of anthrax that would be encountered in a bioweapon (Myers, 1999). They are also critical of the lack of long-term research on the recipients of the vaccine during the Persian Gulf War. The FDA and their

criticism of the vaccine's manufacturer, Bioport, Inc., is not inspiring the military personnel to line up for the vaccine either. These pockets of resistance can significantly affect the readiness of the units, especially with the National Guard and reserve units, who can more easily resign than active duty military personnel (Myers, 1999).

Military Lawsuits Related to the Anthrax Vaccine

Some of these service men and women have filed lawsuits in order to attempt to counteract their dismissal from the military. Perhaps one of the best examples of such a case is Captain John Buck, a 32-year-old emergency room physician, was accused of disobeying an order to take the vaccine before deployment to the Middle East in October of 2000. Buck is arguing that the order to take the anthrax vaccination is not lawful because the administration of an experimental drug would require the consent of the recipient. Rep. Christopher Shays issued a statement on behalf of Buck, and maintained that Buck's choice to refuse the anthrax vaccine because it was not being used in a manner for which it was approved was raising questions, both legal and ethical, about the viability of the anthrax vaccination program. By asking the doctor to take or administer the anthrax vaccine off-label, the military is asking Buck to knowingly violate the Hippocratic oath that he took when he became a doctor (Eberhart, 2001a). Over the course of the court-martial trial, Buck's lawyers have unearthed a great deal of damaging information that will be used against the government. An email from Brig. Gen. Eddie Cain, former director of the Joint Program Office for Biological Defense, states, "I will work the BioPort [anthrax vaccine manufacturer] oversight plan, but believe we are digging ourselves a hole that will be too difficult to crawl out..." (Eberhart, 2001a). According to Shay, Gen. Cain should be fearful, because the vaccine has not been appropriately tested against the routes in which it could be used

in warfare, and concerns that the safety of the vaccine has not been effectively monitored (Eberhart, 2001a). One of the defense witnesses, Dr. Kwai Chan of the General Accounting Office (GAO), had told the House Government Reform Committee in 1999 that the vaccine that the military used to inoculate its members is not the same vaccine that the Pentagon studied for effectiveness (Eberhart, 2001a). Shay maintains “It’s long past time to give up this futile effort to drag a 1950’s medical technology into the 21st century. No one else’s health should be put at risk, and no more military careers should be destroyed on the altar of this unquestionably failed vaccine program” (Eberhart, 2001a). Rep. Dan Burton (R-Ind.), House Government Reform Committee Chairman, has pledged more hearings to push the military into either letting the AVIP program dissolve or making it purely voluntary for the soldiers. He warned, “The Defense Department is giving this investigational vaccine without informed consent. Doing research on our troops without their knowledge or permission is wrong” (FDA says illness, 2000).

Lawmaker Involvement in Anthrax Vaccine Issues

Several lawmakers agree with this assessment, and have been taking action to either ban the use of the vaccine on the military, or at the very least make its use voluntary. In April 2001, Mary Rogeness, Massachusetts State Representative, introduced legislation to prohibit the administration of experimental drugs and vaccines to members of the Massachusetts militia. The bill would force the Massachusetts adjutant general to refrain from administration of any drug or vaccine to any member of the armed services in Massachusetts unless it is licensed by the U.S. Food and Drug administration and used as it is labeled in accordance with the FDA rules and has been proven to be safe and effective through extensive clinical trials (Eberhart, 2001b). Rep. Rogeness began to champion this cause after hearing the case of Capt. Jason M. Nietupski who,

after receiving the anthrax vaccine, has experienced very serious medical problems. Neitupski's medical problems since the anthrax vaccine include chronic fatigue syndrome, liver damage, and blood clots in his leg. These problems began surfacing before he received his third anthrax booster in March 2000. Rogeness hopes that this legislation will overturn the current federal regulations and help the state's military forces (Lauerman, 2001).

Another bill that was introduced was intended to completely do away with the AVIP until the FDA either approves a new vaccine or reduces the boosters on the current vaccine (*Jones Calls*, 1999). Congressman Walter B. Jones (R-NC) is a member of the House Committee on Armed Services, and introduced this legislation (HR 2543) in an attempt to make the AVIP program voluntary for all the members of the U.S military. Jones' bill, called the American Military Health Protection Act, would make the Department of Defense's AVIP program voluntary until certain conditions are met. Jones feels that the concern among our military stems from the fact that there is no clinical study with conclusive results that definitively addresses the long-term side effects of using the anthrax vaccine on human beings. The promises of safety from the Department of Defense have not been backed up with any legitimate support. Jones believes that until the troops are satisfied with the level of information and long-term studies, they should be allowed to make this very important health decision for themselves (*Jones Calls*, 1999).

Rep. Benjamin A. Gilman (NY-20) introduced HR 2548, which is a two-fold legislation to stop the AVIP until the vaccine is proven to be safe and effective, and also to initiate a study by the National Institutes of Health that would further research the anthrax vaccine (*Bill summary*, n.d.). This legislation, formally known as the Department of Defense Anthrax Vaccination Moratorium Act, was introduced on September 19, 1999, and remains referred to the Subcommittee on Health and Environment. This legislation has two primary goals: to express

that “(1) a single protection measure such as the mandatory anthrax vaccine immunization program should not be implemented by the Department of Defense (DOD) without regard to its effect on morale, retention, recruiting, and budget; and (2) an insufficiently proven vaccine should not be advocated as a substitute for research, development, and production of truly effective vaccines and antibiotics, adequate protective equipment, and nonproliferation measures” (*Bill summary*, n.d.). The legislation also requires two things: (1) an independent study of the effectiveness and safety of the vaccine and (2) a report from the Director of the NIH to specified congressional committees on study results. In addition, the bill calls for expedited consideration for former or current military personnel with regard to remedies for adverse personnel actions that were the result of the vaccine program (*Bill summary*, n.d.).

Informed Consent

Informed consent is the process by which an informed individual participates in making decisions about their healthcare. This practice stems from the right for an individual to direct what happens to their body as well as the ethical obligation of the doctor to involve the patient in the healthcare process. A typical informed consent will contain the following components: nature of the decision/procedure, reasonable alternatives to the proposed intervention, any relevant risks, benefits, or uncertainties that are associated with each alternative, a way to assess the patient’s understanding of the procedure, and an indication of acceptance of the risk(s) by the patient. Informed consent is used to ensure that the patient understands the risks and benefits of a particular intervention, such as minor or major surgery. It is also used in experimental medication studies, such as pharmaceutical clinical trials, and is careful to point out that the

patient understands that their participation is voluntary and they can discontinue at any time (Edwards, 1998).

Investigational New Drugs and Informed Consent

In order to administer an investigational new drug (IND) to a research subject, an organization is required to obtain an informed consent. The DoD has been quite compliant with these regulations in the past, however this all changed during the Gulf War. There were two pharmaceuticals that held hopes of being effective against both chemical warfare and biological warfare, and they were both considered to be INDs by the FDA. In order to be in compliance with the FDA's regulations, the DoD would have had to obtain informed consent from every troop to whom they administered these pharmaceuticals, and that did not seem very practical. The DoD also argued that by allowing military personnel to refuse the drugs that were meant for their protection, they could potentially jeopardize combat effectiveness by putting themselves at risk for a disabling infection. The DoD requested that the FDA waive the informed consent requirements and grant waivers for these two pharmaceuticals that were to be used in the Gulf War (*Waiving Informed Consent*, 2000).

The FDA decided that obtaining informed consent from every troop may not be feasible in some of the combat-related scenarios, and that by withholding these INDs, they may be putting more lives at risk by going against the best interests of the military personnel. The FDA put this in writing in what is known as the "Informed Consent for Human Drugs and Biologics; Determination that Informed Consent is Not Feasible". The controversy that ensued was primarily related to the difference between "research" and "treatment." The opponents of the waiver used the argument that an IND is considered to be "research" because the effects, risks,

and potential benefits of the treatment are unknown. In these cases, informed consent is mandatory. In addition, they argued that any organization seeking to have their pharmaceutical in widespread use could change their stated intentions and have an experimental treatment appear to be treatment and completely bypass the informed consent requirements. In contrast, those in favor of the waiver hold that the DoD has an ethical responsibility to protect the members of the military from any potential harm that may come to them while in combat (*Waiving Informed Consent*, 2000).

Due to poor record keeping, less than adequate data collection, and similar violations of the terms of the waiver, the DoD's ability to administer informed consent waivers was questioned. After many years of debate and discussion, the FDA published a "Request for Comments" document in an attempt to determine if the waiver rule should be revoked, changed, or somehow replaced with a form of informed consent for the troops. While the FDA was ready to revoke the waiver rule despite all discussion to the contrary, Congress decided that the waiver capability should reside with the President alone (*Waiving Informed Consent*, 2000). Executive Order 13139, signed in 1999 by then-President Clinton, does not allow the DOD to administer investigational new drugs to service members without their informed consent, except in times of national emergency (Institute for Health Freedom, 2000).

Recommendation

Based on the research performed and the data collected, the most effective solution to this dilemma is to adopt HR-2548, which is Rep. Gilman's legislation that would stop the AVIP until the vaccine is proven safe and efficacious, as well as provide for a NIH study that will further research the vaccine to establish its safety, efficacy, and possible ways to make treatment shorter

or more simple (*Bill Summary*, n.d.). In addition, the bill HR-2543, introduced by Rep. Jones, should be considered because it makes the AVIP voluntary for the military servicemen and women (*Jones Calls*, 1999). These two bills would make it possible to suspend the AVIP pending further research on the current anthrax vaccine, particularly in the arena of inhalation anthrax, and will allow the military personnel to make a personal choice of whether or not they wish to take the vaccine as it is currently offered. The military personnel should all be required to receive and read information regarding the vaccine so that they can make an informed decision on whether or not the vaccine is in their best interest, and can then act accordingly. By making the program voluntary, each soldier would be in control of the medication entering their bodies, and therefore willingly choosing what they feel is in their best interest.

Conclusion

Three principles for determining the ethics of a research protocol were identified in 1978 by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research's Belmont Report. An ethical research protocol will have respect for persons, beneficence, and justice. This is the section of the report that is an issue in the dispute over waiving informed consent for the military. It is well known that by swearing an oath to the military and our country, the personnel in the military are willingly surrendering some of their autonomy regarding their life decisions. However, while this is admirable, should soldiers lose all autonomy, including decisions related to their health? The AVIP was put into place because the DoD believes that the long shot regimen necessitates the vaccination of all of the troops in the event that they face a biological threat. With the current data that raise significant questions regarding the safety and efficacy of the anthrax vaccine, and taking into account the DoD's

recent history with INDs, it is not surprising that many military personnel have doubts about subjecting themselves to the anthrax vaccine (Cummings, n.d.)

As evidenced by several legislative proposals and many advocacy groups, the best way to handle the controversy with the anthrax vaccination would be to make the program voluntary for our military personnel. These men and women risk their lives for our country, and at least deserve the right to determine what experimental substances should be allowed into their bodies. The Association of American Physicians and Surgeons, Inc. (AAPS) advocates that consent cannot be informed if the science is not firm and cannot be backed up with credible research design and data, and that will identify if there are significant adverse effects. The AAPS points out that the entire point of having military personnel sign informed consent forms for vaccines used in combat is not to keep the soldiers from getting the necessary protection, but to let them decide whether or not they feel the potential risks are worth the potential benefits (Orient, 1999).

According to the Department of Defense, informed consent from members of the military is not necessary before administering the anthrax vaccine. The official website maintained by the DOD states that the vaccine is fully licensed by the FDA and consent is therefore not required. Those receiving the vaccine will be given vaccine information, and may request it anytime after vaccination (*AVIP*, n.d.). However, the military personnel that are being ordered to take this vaccine must choose between obeying a direct order and putting a substance into their bodies that could potentially do more harm than good. Once military service is complete, the uniform is left behind, however the anthrax vaccine remains forever. Many of our men and women in uniform did not realize they were making that kind of commitment when they enlisted in the military (*One Hundred Sixth Congress*, 1999).

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